Pearls & Oy-sters: Bilateral globus pallidus lesions in a patient with COVID-19

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Pearls

- Neurologic complications are occurring in coronavirus disease 2019 (COVID-19), and these patients should be monitored for neurologic symptoms.
- When evaluating abnormal imaging findings in patients with COVID-19, the presence and specific pattern of deep gray structure involvement can be an important clue to etiology.

Oy-sters

- Brain imaging should be considered in the context of patients with COVID-19 with neurologic symptoms, even in the absence of focal findings on neurologic examination.
- Given the dissociation between degree of hypoxemia and clinical symptoms that can be seen in patients with COVID-19, it is possible that unusual presentations of hypoxic–ischemic brain injury may emerge.

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COVID-19, caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was originally described as a viral infection primarily affecting the respiratory tract. Neurologic complications are emerging, and have been reported in 36% of patients hospitalized with COVID-19 and in 46% of those with severe respiratory involvement.[1] The most common neurologic manifestations reported are dizziness, headache, impaired consciousness, dysgeusia, and hyposmia. An increased risk of stroke has also been identified.

We report the case of a 52-year-old woman with bilateral globus pallidus lesions in the setting of COVID-19. The patient had a history of hypertension and newly diagnosed, poorly controlled type II diabetes mellitus (hemoglobin A1c of 17.4). She developed bilateral hand paresthesias the week prior to presentation, followed by dyspnea, cough, headache, and confusion. She presented to the emergency department and was afebrile, but tachycardic (115 beats per minute), hypertensive (220/118 mm Hg), and hypoxemic (oxygen saturation 49% on room air). She was alert and conversant, with no focal neurologic deficits. She had refractory hypoxemia despite 20 L/min supplemental oxygen. She was intubated and placed on mechanical ventilation for hypoxemic respiratory failure within 1 hour of presentation. SARS-CoV-2 was detected by rapid, real-time reverse-transcriptase polymerase chain reaction on the Cepheid GeneXpert system from a nasopharyngeal swab sample. Chest CT scan showed extensive bilateral, patchy, peripheral-predominant ground glass opacities with consolidation. Head CT demonstrated symmetric hypoattenuation in the bilateral globi pallidi with surrounding small foci of hyperattenuation (figure, A). Carboxyhemoglobin was not elevated and urine toxicology screen was negative.

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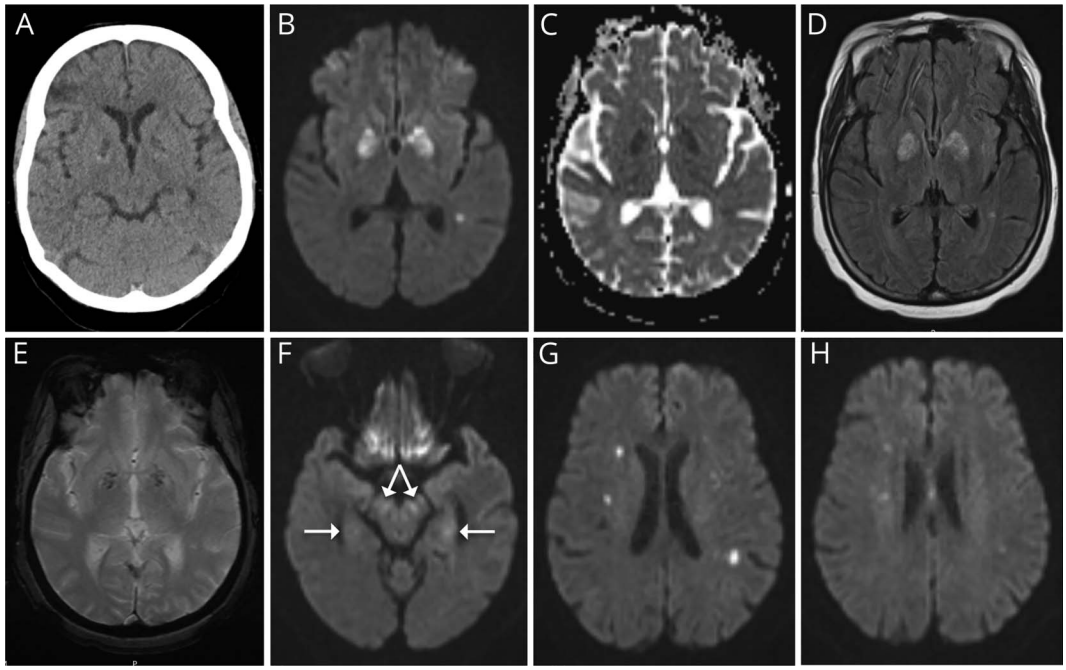
Figure Multifocal lesions on head CT and brain MRI



Initial head CT demonstrating symmetric hypoattenuation in the bilateral globi pallidi with surrounding small foci of hyperattenuation (A). Brain MRI on hospital day 8, showing bilateral lesions in the globi pallidi (B–E). Injury is characterized by diffusion restriction (B and C show diffusion-weighted imaging [DWI] and apparent diffusion coefficient sequences, respectively), symmetric T2/fluid-attenuated inversion recovery prolongation (D), and foci of decreased signal on gradient echo sequence (E). There was also subtle restricted diffusion and abnormal T2 prolongation in the left greater than right hippocampus (F, single arrows) and substantia nigra (F, double arrow). Also visualized were scattered punctate, acute infarcts in the bilateral cerebral white matter and corpus callosum (G and H; DWI).

Upon presentation, the patient was in a hyperglycemic crisis that had features of both diabetic ketoacidosis and hyperosmolar hyperglycemic state (glucose 1,114 mg/dL, anion gap 33, β-hydroxybutyrate 4.02 mmol/L, peripheral venous pH 7.25). She was in shock, with lactate of 7.7 mmol/L, low central venous saturation (52%), and elevated troponin and NT-proBNP. Point of care ultrasound showed signs of right ventricular failure and 4-extremity venous duplex visualized a right subclavian deep vein thrombosis, and she was diagnosed with obstructive shock due to presumed pulmonary embolism. Laboratory studies in the first 24 hours of hospitalization were concerning for disseminated intravascular coagulation with elevated D-dimer (>128 ug/mL fibrinogen equivalent units), low fibrinogen (nadir of 66 mg/dL), and thrombocytopenia (52,000 per μL). She was started on a continuous heparin infusion, and repeat head CT on hospital day 3 remained stable with no evidence of new or increasing hemorrhage. Her course was complicated by acute kidney injury requiring continuous renal replacement therapy, shock liver, and ventilator-associated pneumonia.

The patient's mental status remained poor on hospital day 8 despite weaning sedation; she was intubated on pressure support, opened her eyes to noxious stimulation, and localized to pain, but did not follow commands. Brainstem reflexes were intact and she moved all extremities spontaneously. A brain MRI was obtained, which demonstrated symmetric T2 prolongation in the bilateral globi pallidi, with associated diffusion restriction and foci of decreased signal on gradient echo sequence, at least some of which was suggestive of blood products (i.e., not all clearly mineral on CT; figure, B–E). Faint restricted diffusion and abnormal T2 prolongation were noted in the left greater than right hippocampus as well as substantia nigra (figure, F). Scattered punctate, acute–subacute infarcts were evident in the bilateral cerebral white matter and corpus callosum, with a possible watershed distribution (figure, G and H). There was no pathologic enhancement except for one mildly enhancing right cerebellar subacute infarct. Other deep gray nuclei were spared. Lumbar puncture was deferred due to the need for continued anticoagulation in the setting of pulmonary embolism. Vascular imaging was also deferred.

Discussion

The primary differential diagnostic considerations for bilateral pallidal lesions included hypoxia and COVID-19–associated acute hemorrhagic necrotizing encephalopathy. Carbon monoxide poisoning and other toxic etiologies were unlikely given the patient's clinical history and laboratory findings. Scattered bilateral acute infarcts may have been related to hypercoagulability or embolic phenomena.

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As COVID-19 is a novel disease, there are few reports of neurologic sequelae. To date, one case of COVID-19–associated acute hemorrhagic necrotizing encephalopathy has been reported, with a pattern of predominantly thalamic involvement that is characteristic of acute necrotizing encephalopathy (ANE) associated with other viral illnesses.[2] This is thought to result from intracranial cytokine storm with blood–brain barrier breakdown leading to symmetric, multifocal lesions involving the thalamus.[3] In our patient, the thalami were spared and the bilateral globi pallidi were severely affected with abnormal signal in the substantia nigra, which is not entirely consistent with prior reports of ANE.

Another consideration is hypoxic–ischemic injury. This patient's imaging is similar to the pattern seen in hypoxic–ischemic injury, including bilateral pallidal lesions and hippocampal involvement.[4] However, hypoxic–ischemic injury is generally associated with involvement of other superficial and deep gray structures, which was not observed in our patient.[5] Whereas our patient was profoundly hypoxemic and in shock upon presentation, she did not have a cardiopulmonary arrest or other event likely to cause frank global anoxia/ischemia, and findings in the globi pallidi were evident on the initial CT within hours of uncomplicated intubation. On the other hand, given anecdotal reports of patients with COVID-19 presenting with severe hypoxemia seemingly out of proportion to their relatively well-preserved lung mechanics[6] and overall clinical appearance, it may be possible that these patients could endure severe enough hypoxia to cause hypoxic brain injury in the absence of cardiopulmonary arrest.

A confounding factor in the diagnosis of this patient's brain injury was the fact that she presented with a hyperglycemic crisis. Hyperglycemia is known to cause injury to the basal ganglia, but typically affects the caudate and/or putamen with hyperdensity on CT and intrinsic T1 hyperintensity on MRI, which were absent in this case.[7] Whereas this patient's imaging was not consistent with hyperglycemic changes alone, the presence of severe hyperglycemia may have rendered the metabolically vulnerable globi pallidi even more susceptible to other insults, such as hypoxia.

Taken together, we propose that our patient's clinical case is most consistent with hypoxic–ischemic brain injury in the setting of COVID-19 infection, in the absence of a cardiopulmonary arrest. Given the dissociation between degree of hypoxemia and clinical symptoms seen in both our patient and other patients with COVID-19, it is plausible that sustained, profound hypoxemia over hours to days prior to presentation may lead to hypoxic–ischemic brain injury in these patients, even without cardiopulmonary arrest. In our patient, this vulnerability may have been exacerbated by the additional metabolic insult of her hyperglycemic crisis. In the context of mounting evidence of neurologic complications of COVID-19, brain imaging should be considered when these patients present with neurologic symptoms. Additional studies will be needed to fully understand the spectrum of neurologic complications associated with COVID-19.

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Disclosure

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Appendix Authors

Name	Location	Contribution
Catherine V. Kulick-Soper, MD	University of Pennsylvania, Philadelphia	Study concept and design, major role in acquisition of data, interpretation of data, literature review, drafted the manuscript for intellectual content, revised the manuscript for intellectual content
Jillian L. McKee, MD, PhD	University of Pennsylvania and The Children's Hospital of Philadelphia	Study concept and design, major role in acquisition of data, interpretation of data, literature review, drafted the manuscript for intellectual content, revised the manuscript for intellectual content
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Joel M. Stein, MD, PhD	University of Pennsylvania, Philadelphia	Interpretation of data, revised the manuscript for intellectual content
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Ross N. England, MD	University of Pennsylvania, Philadelphia	Interpretation of data, revised the manuscript for intellectual content
Aaron Rothstein, MD	University of Pennsylvania, Philadelphia	Interpretation of data, revised the manuscript for intellectual content

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Appendix *(continued)*

Name	Location	Contribution
Michael A. Gelfand, MD, PhD	University of Pennsylvania, Philadelphia	Interpretation of data, revised the manuscript for intellectual content
Brett L. Cucchiara, MD	University of Pennsylvania, Philadelphia	Interpretation of data, revised the manuscript for intellectual content
Kathryn A. Davis, MD	University of Pennsylvania, Philadelphia	Study concept and design, major role in acquisition of data, interpretation of data, revised the manuscript for intellectual content

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